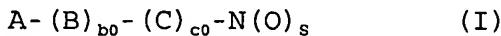


CLAIMS

1. Use for the preparation of disease-modifying drugs drugs for the prevention and treatment of arthritis therapy of compounds or salts thereof having the following general formula:



wherein:

s is an integer and is equal to 1 or 2, preferably 2;
 c0 is an integer and is equal to 0 or 1;
 b0 is an integer and is 0 or 1; with the proviso that at least one between c0 and b0 is different from zero;

A = R-T₁-, wherein

R- is the radical of a non steroidal antiinflammatory precursor drug excluding the compounds having 2-oxo-1H-indolic structure, or the radical of a non steroidal antiinflammatory/analgesic drug;

T₁ = (CO)_t or (X)_{t'}, wherein X = -O-, -S-, -N(R_{1c})-, R_{1c} is H or C₁-C₅ linear or branched alkyl, t and t' are integers and equal to zero or 1, with the proviso that t = 1 when t' = 0; t = 0 when t' = 1;

B = -T_B-X₂-T_{BI}- wherein

T_B and T_{BI} are equal or different;

T_B = (CO) when the reactive function in the precursor drug is -OH or -NH(R_{1c}); T_B = X, as above, when the reactive function in the precursor drug is -COOH;

T_{BI} = (CO)_{tx} or (X)_{txx}, wherein tx and txx have the value of 0 or 1; with the proviso that tx = 1 when txx = 0, tx = 0 when txx = 1; X is as above;

X₂ is a bivalent linking group as defined below;

C is the bivalent radical -T_c-Y- wherein

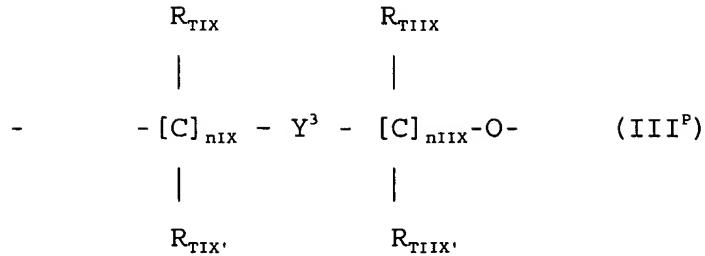
when b0 = c0 = 1: T_c = (CO) when tx = 0, T_c = X when txx = 0, X being as above;

when b0 = 0: T_c = (CO) when t = 0, T_c = X when t' = 0, X being as above;

when $c_0 = 0$: $tx = 0$, $T_{BI} = X = -O-$.

Y is:

Y_p :



wherein:

nIX is an integer from 0 to 10, preferably from 1 to 3;

$nIIIX$ is an integer from 1 to 10, preferably from 1 to 3;

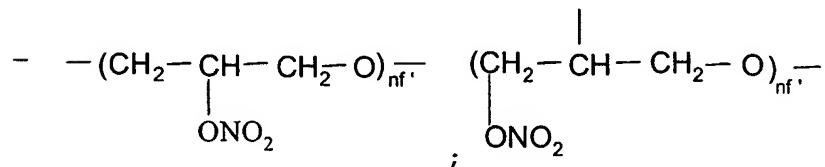
R_{TIX} , $R_{TIX'}$, R_{TIIIX} , $R_{TIIIX'}$, equal to or different from each other are H or C_1-C_4 linear or branched alkyl; preferably R_{TIX} , $R_{TIX'}$, R_{TIIIX} , $R_{TIIIX'}$ are H.

Y^3 is a saturated, unsaturated or aromatic heterocyclic ring containing one or two nitrogen atoms having 5 or 6 atoms,

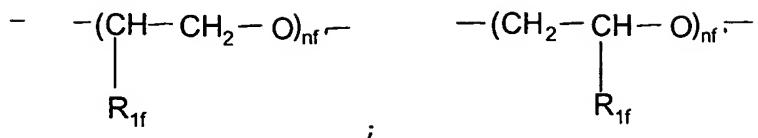
or Y can be:

Y_0 , selected from the following:

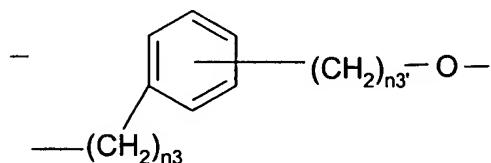
- a $-R'O-$ alkylenoxy group wherein R' is linear or branched when possible C_1-C_{20} , preferably having from 2 to 6 carbon atoms, or a cycloalkylene having from 5 to 7 carbon atoms, in the cycloalkylene ring one or more carbon atoms can be substituted by heteroatoms, the ring can have side chains of R' type, R' being as above; or one of the following groups:



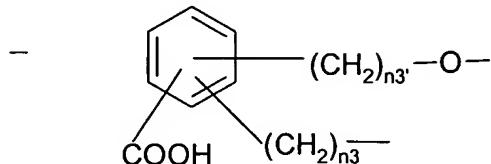
wherein nf' is an integer from 1 to 6 preferably from 1 to 4;



wherein $R_{1f} = H, CH_3$ and nf' is an integer from 1 to 6; preferably from 1 to 4;
or Y is Y_{Ar} and is selected from the following:



wherein $n3$ is an integer from 0 to 3 and $n3'$ is an integer from 1 to 3;



wherein $n3$ and $n3'$ have the above meaning;
 X_2 , bivalent radicalm is such that the corresponding precursor of B , $-T_B-X_2-T_{BI}-$ wherein the free valences of T_B and of T_{BI} are saturated each with OZ , with Z or with $-N(Z^I)(Z^{II})$, wherein $Z = H, C_1-C_{10}$, preferably C_1-C_5 linear or branched when possible alkyl, Z^I, Z^{II} equal or different have the Z values as above, depending on that T_B and/or $T_{BI} = CO$ or X , in function of the values of t, t', tx and txx ;

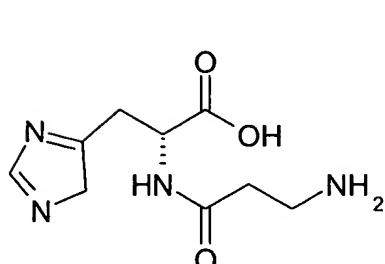
the precursor of B is selected from the following:

- aminoacids,
- hydroxyacids,
- aromatic and heterocyclic mono- and polyalchols,

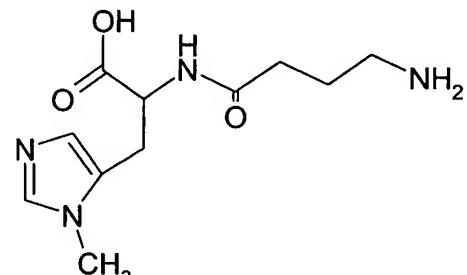
- compounds containing at least one free acid function.

2. Use according to claim 1, wherein the precursor of B is selected from the following:

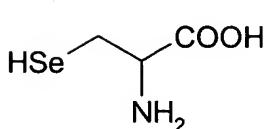
- aminoacids selected from the following: L-carnosine (formula CI), anserine (CII), selenocysteine (CIII), selenomethionine (CIV), penicillamine (CV), N-acetylpenicillamine (CVI), cysteine (CVII), N-acetylcysteine (CVIII), glutathione (CIX) or esters thereof, preferably ethyl or isopropyl ester:



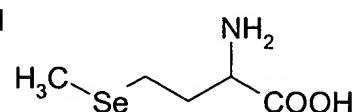
(CI)



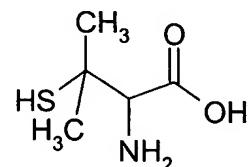
(CII)



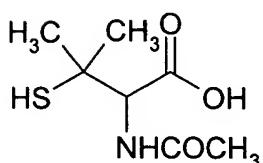
(CIV)



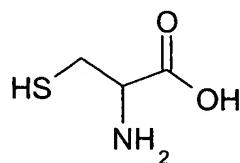
(CIII)



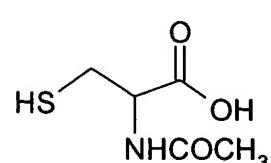
(CV)



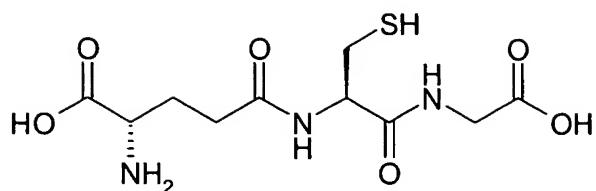
(CVI)



(CVII)

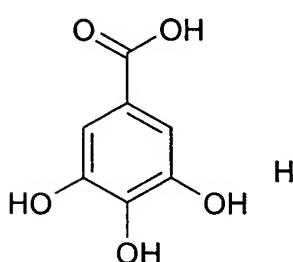


(CVIII)

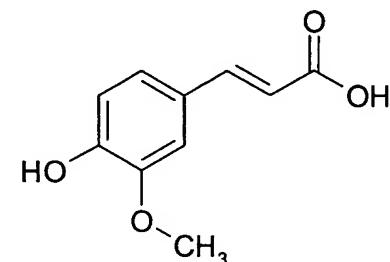


(CIX)

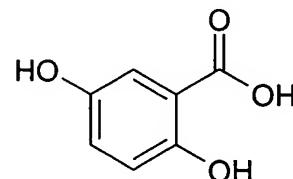
- hydroxyacids, selected from the following: gallic acid (formula DI), ferulic acid (DII), gentisic acid (DIII), citric acid (DIV), caffeic acid (DV), dihydrocaffeic acid (DVI), p-cumaric acid (DVII), vanilllic acid (DVIII):



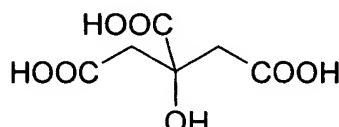
(DI)



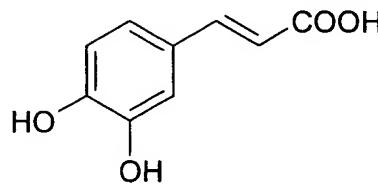
(DII)



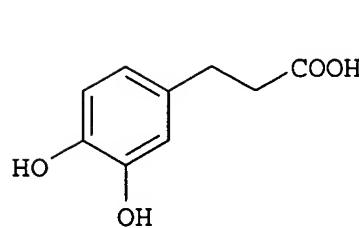
(DIII)



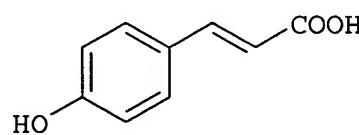
(DV)



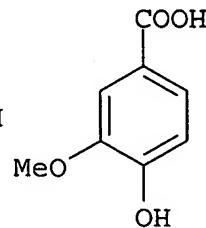
(DV)



(DVI)



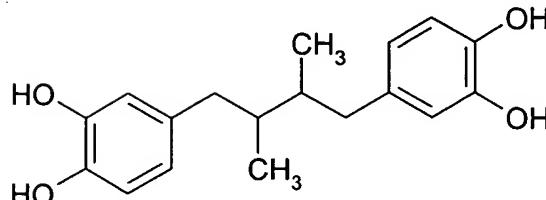
(DVII)



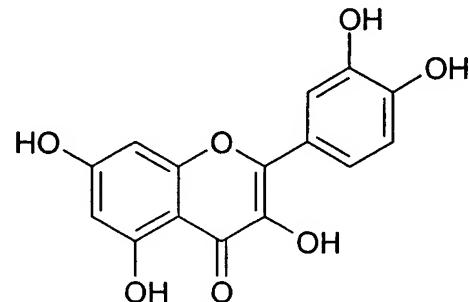
(DVIII)

- aromatic and heterocyclic mono- and polyalcohols, selected from the following: nordihydroguaiaretic acid (EI), quercetin (EII), catekin (EIII), kaemp-

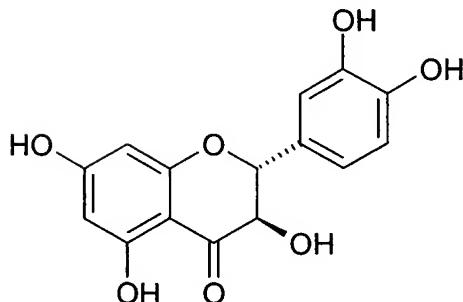
ferol (EIV), sulphurethyne (EV), hydroquinone (EVIII), gossypol (EIX), reductic acid (EX), methoxyhydroquinone (EXI), hydroxyhydroquinone (EXII), propyl gallate (EXIII), 3,5-di-ter-butyl-4-hydroxybenzyl-thioglycolate (EXXIV), allopurinol (EXXXI); saccharose (EC), ascorbic (ECI) and isoascorbic acid (ECII), p-cumaric alcohol (ECIII), 4-hydroxy-phenylethylalcohol (ECIV), coniferyl alcohol (ECV) :



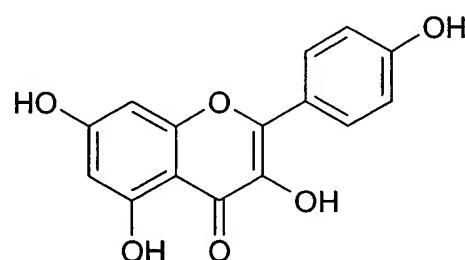
(EI)



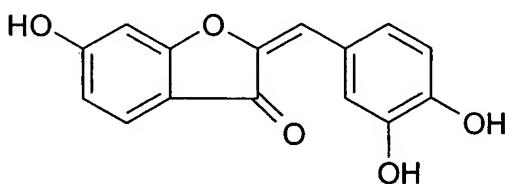
(EIII)



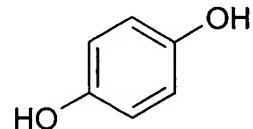
(EIV)



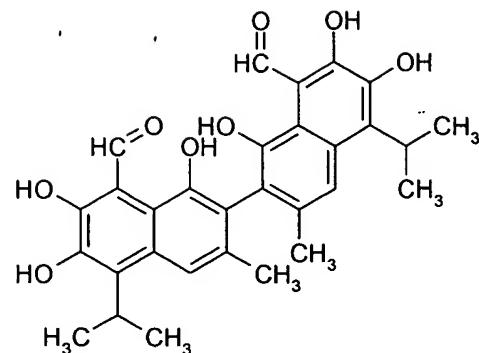
(EV)



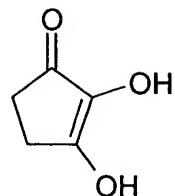
(EVIII)



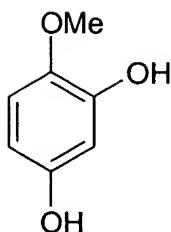
(EVIII)



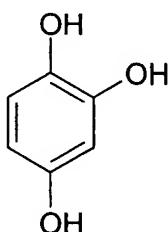
(EIX)



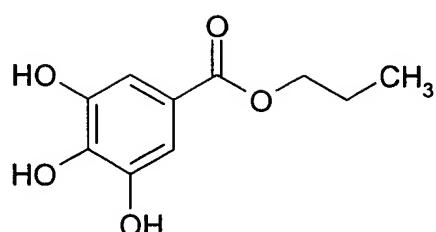
(EX)



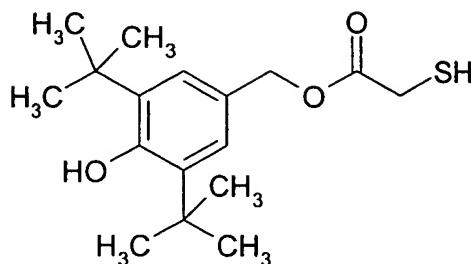
(EXI)



(EXII)



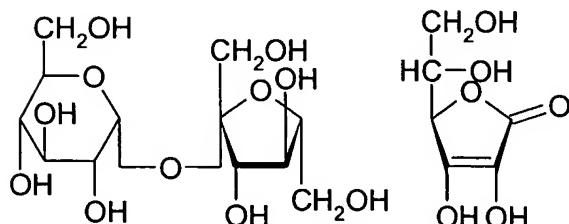
(EXIII)



(EXXIV)



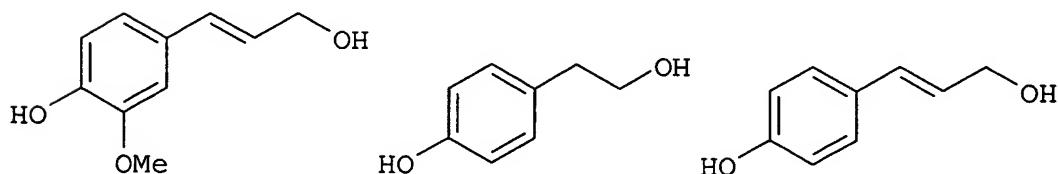
(EXXXI)



(EC)

(ECI)

(ECII)

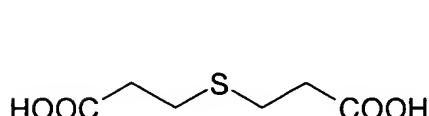


(ECIII)

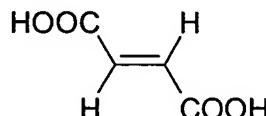
(ECIV)

(ECV)

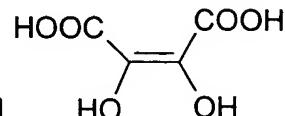
- compounds containing at least one free acid function, selected from the following: 3,3'-thiodipropionic acid (NI), fumaric acid (NII), dihydroxymaleic acid (NIII), edetic acid (NV) :



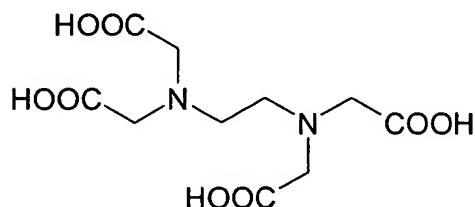
(NI)



(NII)



(NIII)

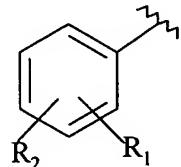


(NV)

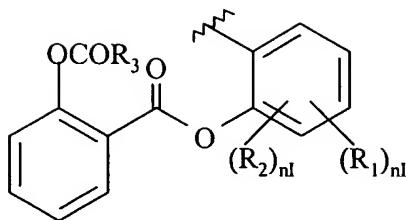
3. Use according to claims 1-2, wherein in the compounds of formula (I) when $b_0 = c_0 = 1$, the bonds between the drug radical and X_2 and between X_2 and Y are, independently the one from the other, of ester, thioester, amide type; when $b_0 = 0$ and $c_0 = 1$ the bond between the drug radical and Y is of ester, thioester, amide type.
4. Use according to claims 1-3, wherein the R radical is selected from the following groups:

Group I)

Ia)



Ib)



wherein:

R_1 is H or $-\text{OCOR}_3$; wherein R_3 is methyl, ethyl or $C_3\text{-}C_5$ linear or branched alkyl, or the residue of an heterocycle with only one ring having 5 or 6 atoms partially or totally hydrogenated, or aromatic, containing one or more heteroatoms independently selected from O, N and S;

R_2 is hydrogen, hydroxy, halogen, $C_1\text{-}C_4$ linear or branched alkyl, $C_1\text{-}C_4$ linear or branched alkoxy; a $C_1\text{-}C_4$ linear or branched perluoroalkyl, for example trifluoromethyl; nitro, amino, mono- or di- (C_{1-4}) alkylamino;

with the proviso that in formula Ia) R_1 and R_2 are not contemporaneously H; preferably when $R_1 = \text{H}$ $R_2 = \text{OH}$;
preferably in the compounds of formula Ia) $T_1 = -\text{CO-}$ and:

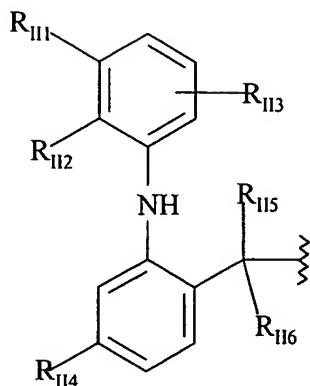
- R_1 = acetoxy, preferably in ortho position with respect to $-\text{CO-}$, R_2 is hydrogen; in this case the formula Ia) represents the acetylsalicylic acid residue;
- $R_1 = \text{H}$ $R_2 = \text{OH}$, preferably in ortho position with respect to $-\text{CO-}$, in this case the formula Ia) represents the salicylic acid residue;

in formula Ib) nI is an integer 0 or 1;

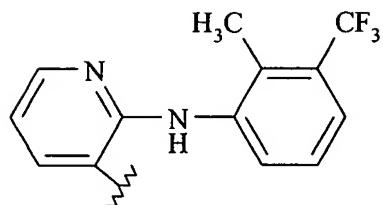
preferably in the compounds of formula Ib) $R_3 = \text{CH}_3$, $nI = 0$, $T_1 = -\text{CO-}$; in this case Ib) is the acetylsalicylsalicylic acid residue;

Group II)

IIa)



IIb)



wherein:

R_{II5} is H, C_1-C_3 linear or branched when possible alkyl;

R_{II6} has the same meaning as R_{II5} , or when R_{II5} is H it is benzyl;

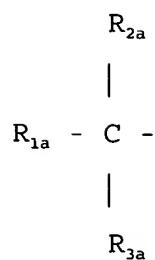
R_{II1} , R_{II2} and R_{II3} are independently hydrogen, C_1-C_6 linear or branched alkyl, or C_1-C_6 linear or branched alkoxy, or Cl, F, Br;

R_{II4} is R_{II1} or bromine;

the compounds are preferred wherein R_{II1} , R_{II4} are hydrogen and R_{II2} and R_{II3} are chlorine in ortho position with respect to NH; R_{II5} and R_{II6} are H, $T_1 = -CO-$, when the free valence is saturated with OH the precursor compound is known as diclofenac.

IIb) is the residue of the 2-[(2-methyl-3-(trifluoromethyl)phenyl)amino]-3-pyridincarboxylic acid when $T_1 = -CO-$ and the free valence is saturated with OH the compound is known as flunixin;

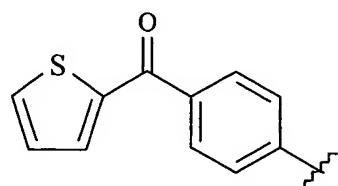
Group III) wherein R is:



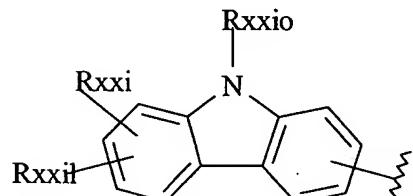
wherein:

R_{2a} and R_{3a} are H, C₁-C₁₂ linear or branched, substituted or not, alkyl or allyl, with the proviso that when one of the two is allyl the other is H; preferably R_{2a} and R_{3a} , equal or different, are H, C₁-C₄ alkyl;

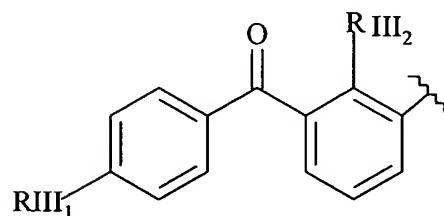
R_{1a} is selected from:



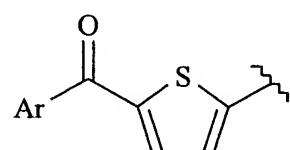
(II)



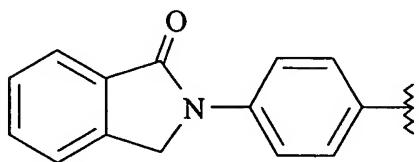
(XXI)



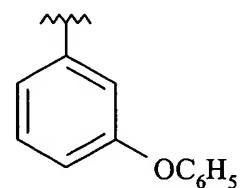
(IV)



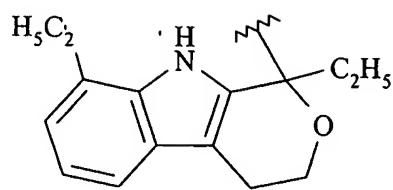
(XXXV)



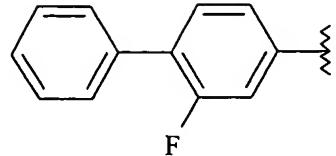
(VI)



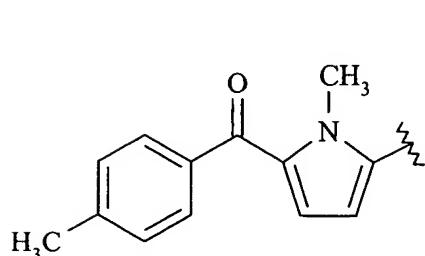
(VII)



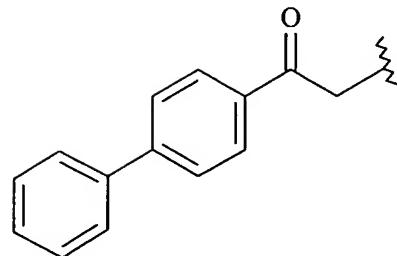
(VIII)



(IX)

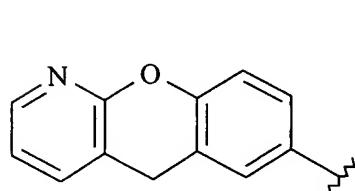


(X)

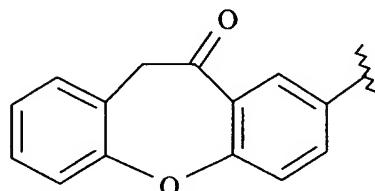


(III)

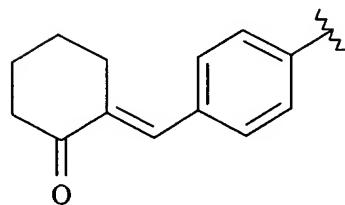
IIID) R_{1a} corresponds to the following formulas:



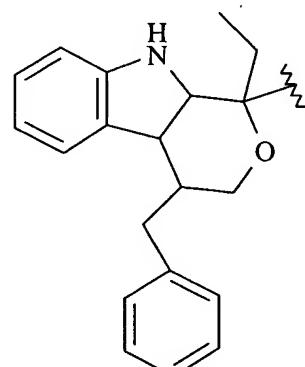
(IIIa)



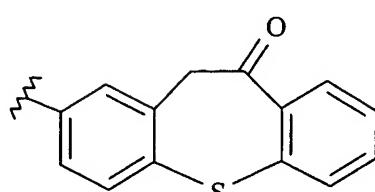
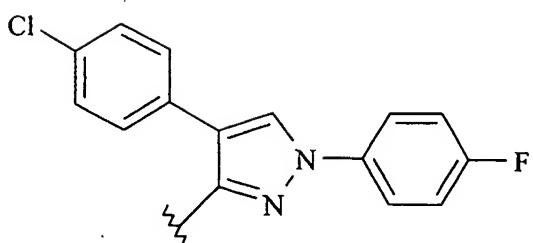
(XXX)



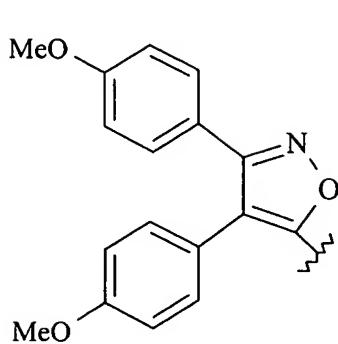
(XXXI)



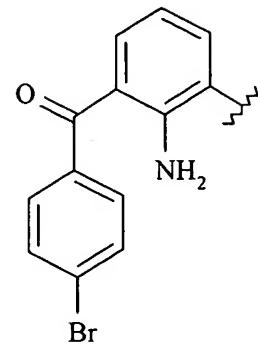
(XXXII)



(XXXIII)

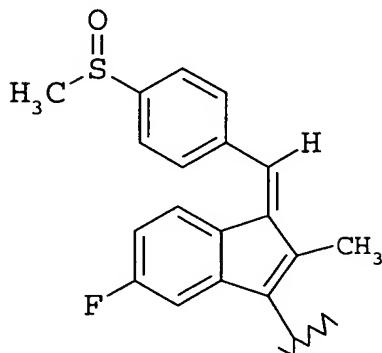


(XXXVI)



(XXXVIII)

(XII)



(XXXX)

wherein the meanings are the following:

- when R_{1a} is as defined in formula (IV), Ketoprofen residue:
 - R_{III1} is H, SR_{III3} wherein R_{III3} is C_1 - C_4 linear or branched alkyl;
 - R_{III2} is H, hydroxy;
 - the compounds wherein R_{III1} and R_{III2} are H, R_{3a} is H, and R_{2a} is methyl, $T_1 = -CO-$ are preferred;
- when R_{1a} is as defined in formula (XXI), carprofen residue:
 - R_{xxio} is H, alkyl from 1 to 6 C atoms linear or branched, C_1 - C_6 alkoxy carbonyl linked to a C_1 - C_6 alkyl, C_1 - C_6 carboxy alkyl, C_1 - C_6 alkanoyl, optionally substituted with halogens, benzyl or halobenzyl, benzoyl or halobenzoyl;

R_{xxi} is H, halogen, hydroxy, CN, C_1 - C_6 alkyl containing or not containing OH groups, C_1 - C_6 alkoxy, acetyl, benzyloxy, SR_{xxi2} wherein R_{xxi2} is C_1 - C_6 alkyl; C_1 - C_3 perfluoroalkyl; C_1 - C_6 carboxyalkyl containing or not containing OH groups, NO_2 , amino; sulphamoyl, di-alkyl sulphamoyl with C_1 - C_6 alkyl, or di-fluoroalkylsulphonyl with C_1 - C_3 alkyl;

R_{xxi1} is halogen, CN, C_1 - C_6 alkyl containing one or more OH groups, C_1 - C_6 alkoxy, acetyl, acetamido, benzyloxy, SR_{III3} being R_{III3} as above, C_1 - C_3 perfluoroalkyl, hydroxy, C_1 - C_6 carboxyalkyl, NO_2 , amino, C_1 - C_6 mono- or di-alkyl-amino; sulphamoyl, C_1 - C_6 di-alkylsulphamoyl, or di-fluoroalkylsulphamoyl as above; or R_{xxi} together with R_{xxi1} is a C_1 - C_6 alkylen-dioxy; the compounds are preferred wherein R_{xxi0} is H, the linking group is in position 2, R_{xxi} is H, R_{xxi1} is chlorine and is in para position with respect to the nitrogen;

R_{3a} is H, R_{2a} is methyl and $T_1 = -CO-$;

- when R_{1a} is as defined in formula (XXXV) tiaprofenic acid residue:

Ar is phenyl, hydroxyphenyl optionally mono- or polysubstituted with halogen, alkanoyl and C_1 - C_6 alkoxy, C_1 - C_6 trialkyl, preferably C_1 - C_3 , cyclopentyl, cyclohexyl, cycloheptyl, heteroaryl, preferably thienyl, furyl containing or not containing OH, pyridyl;

the preferred compounds of (XXXV) are those wherein Ar is phenyl, R_{3a} is H, R_{2a} is methyl and $T_1 = -CO-$;

- when R_{1a} is as defined in formula (II), suprofen residue, R_{3a} is H, R_{2a} is methyl and $T_1 = -CO-$;

- when R_{1a} is as defined in formula (VI), R is the residue of indoprofen when $T_1 = -CO-$, $R_{2a} = H$ and R_{3a}

= CH_3 ; of indobufen when R_{2a} is equal to H and R_{3a} = C_2H_5 ; T_1 = -CO-;

- when R_{1a} is as defined in formula (VIII), R is the etodolac residue when R_{2a} = R_{3a} = H and T_1 = -CO-;
- when R_{1a} is as defined in formula (VII), R is the fenoprofen residue when R_{3a} = H, R_{2a} = CH_3 and T_1 = -CO-;
- when R_{1a} is as defined in formula (III), R is the fenbufen residue when R_{2a} = R_{3a} = H and T_1 = -CO-;
- when R_{1a} is as defined in formula (IX), R is the flurbiprofen residue when R_{3a} = H, R_{2a} = CH_3 , T_1 = -CO-;
- when R_{1a} is as defined in formula (X) R is the tolmetin residue when R_{2a} = R_{3a} = H, T_1 = -CO-.

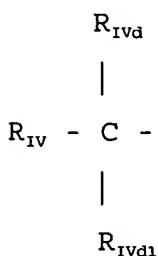
In group IIID) R_{1a} corresponds to the following formulas:

- IIIa), when R_{2a} = H and R_{3a} = CH_3 the pranoprofen residue is obtained: α -methyl-5H-[1]benzopyran-[2,3-b]pyridin-7-acetic acid; in the preferred compound R_{2a} = H, R_{3a} = CH_3 , T_1 = -CO- and in the precursor the free valence is saturated with OH;
- (XXX), when R_{2a} = H and R_{3a} = CH_3 the bermoprofen residue is obtained: dibenz[b,f]oxepin-2-acetic acid; in the preferred compound R_{2a} = H, R_{3a} = CH_3 , T_1 = -CO-;
- (XXXI), when R_{2a} = H and R_{3a} = CH_3 , R is the radical of the compound CS-670: 2-[4-(2-oxo-1-cyclohexyliden methyl) phenyl]propionic acid; the preferred compound has R_{2a} = H, R_{3a} = CH_3 , T_1 = -CO-;
- (XXXII), when R_{2a} = R_{3a} = H, the pemedolac residue is obtained; when R_{2a} = R_{3a} = H T_1 = -CO-;
- (XXXIII), when R_{2a} = R_{3a} = H, the pirazolac residue is obtained: 4-(4-chlorophenyl)-1-(4-fluorophenyl)-3-pyrazol acid derivatives;

the preferred compounds have R_{2a} = R_{3a} = H, T_1 = -CO-;

- (XXXVI), when $R_{2a} = H$, $R_{3a} = CH_3$ the zaltoprofen residue is obtained; when the residue is saturated with an hydroxyl or aminic group, or with the carboxylic function the compounds are known as dibenzotiepin derivatives; in the preferred compounds $R_{2a} = H$, $R_{3a} = CH_3$, $T_1 = -CO-$;
- (XXXVII), when $R_{2a} = R_{3a} = H$ the mofezolac residue is obtained: 3,4-di(p-methoxyphenyl)isoxazol-5-acetic acid when the residue is CH_2-COOH ; in the preferred compounds $R_{2a} = R_{3a} = H$, $T_1 = -CO-$;
- (XII), when $R_{2a} = R_{3a} = H$ the bromfenac residue is obtained: 2-amino-3-(4-bromobenzoyl)benzeneacetic acid; the preferred compounds have $T_1 = -CO-$, $R_{2a} = R_{3a} = H$;
- (XXXX) when $R_{2a} = R_{3a} = H$ the sulindac residue is obtained: (Z)-5-fluoro-2-methyl-1-[(4-(methylsulphinyl)-phenyl)methylene]-1H-inden-3-acetic acid; the preferred compounds have $T_1 = -CO-$, $R_{2a} = R_{3a} = H$;

in Group IV) R is

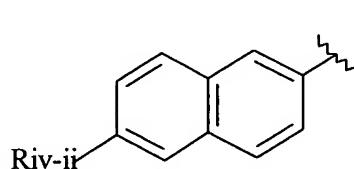


wherein:

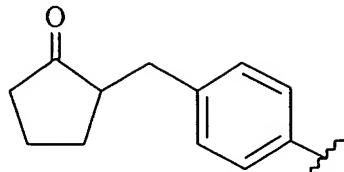
R_{IVd} and R_{IVd1} are at least one H and the other an alkyl from C_1 to C_6 linear or branched, preferably C_1-C_2 , or di-

fluoroalkyl with C₁-C₆ alkyl, C₁ preferred, or R_{IVd} and R_{IVd1} form together a methylene group;

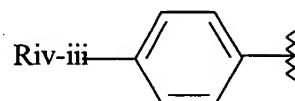
R_{IV} has the following meaning;



(IIB)



(XB)



(IIIB)

wherein the compounds of group IV) have the following meanings:

- in formula (IIB):

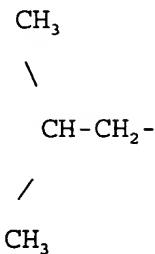
R_{IV-ii} is C₁-C₆ alkyl, C₃-C₇ cycloalkyl, C₁-C₇ alkoxyethyl, C₁-C₃ trifluoroalkyl, vinyl, ethynyl, halogen, C₁-C₆ alkoxy, difluoroalkoxy with C₁-C₇ alkyl, C₁-C₇ alkoxyethoxy, alkylthiomethoxy with C₁-C₇ alkyl, alkyl methylthio with C₁-C₇ alkyl, cyano, difluoromethylthio, phenyl- or phenylalkyl substituted with the C₁-C₆ alkyl; preferably R_{IV-ii} is CH₃O-, R_{IVd} is H and R_{IVd1} is CH₃, and is known as naproxene residue; T₁ = -CO-;

- in formula (XB), of which the loxoprofen residue has been indicated, the compounds wherein R_{IVd} is H and R_{IVd1} is CH₃, T₁ = -CO- are preferred;

- in formula (IIIB):

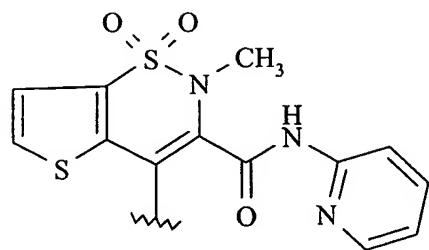
R_{IV-iii} is a C₂-C₅ branched or not branched alkyl, C₂ and C₃ alkyloxy, allyloxy, phenoxy, phenylthio, cycloalkyl from 5 to 7 C atoms, optionally substituted in position 1 by a C₁-C₂ alkyl;

the compound is preferred wherein $R_{iv,iii}$ is

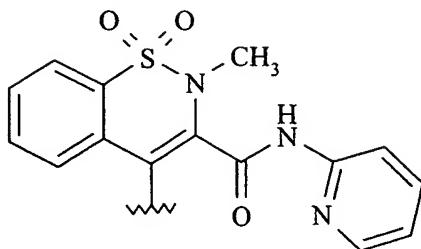


and $R_{IVd} = H$, R_{IVd1} is CH_3 , compound known as ibuprofen residue, $T_1 = -CO-$;

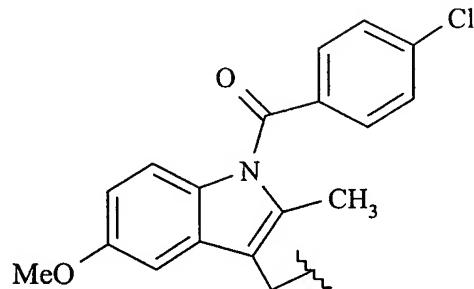
Group V)



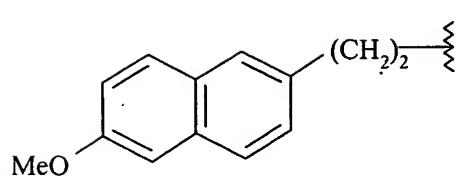
(VIIC)



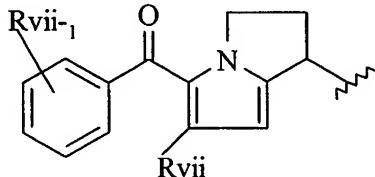
(IXC)



(IVC)

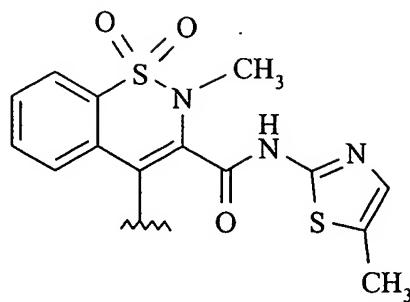


(IIIc)

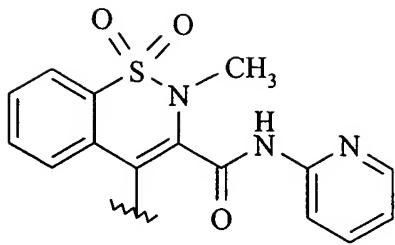


(IIC)

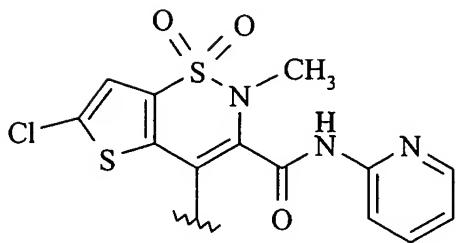
Group VE)



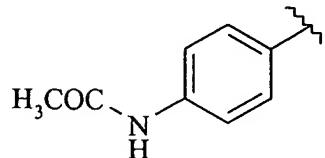
(xc)



(xi)



(XIII)



(xxxxv)

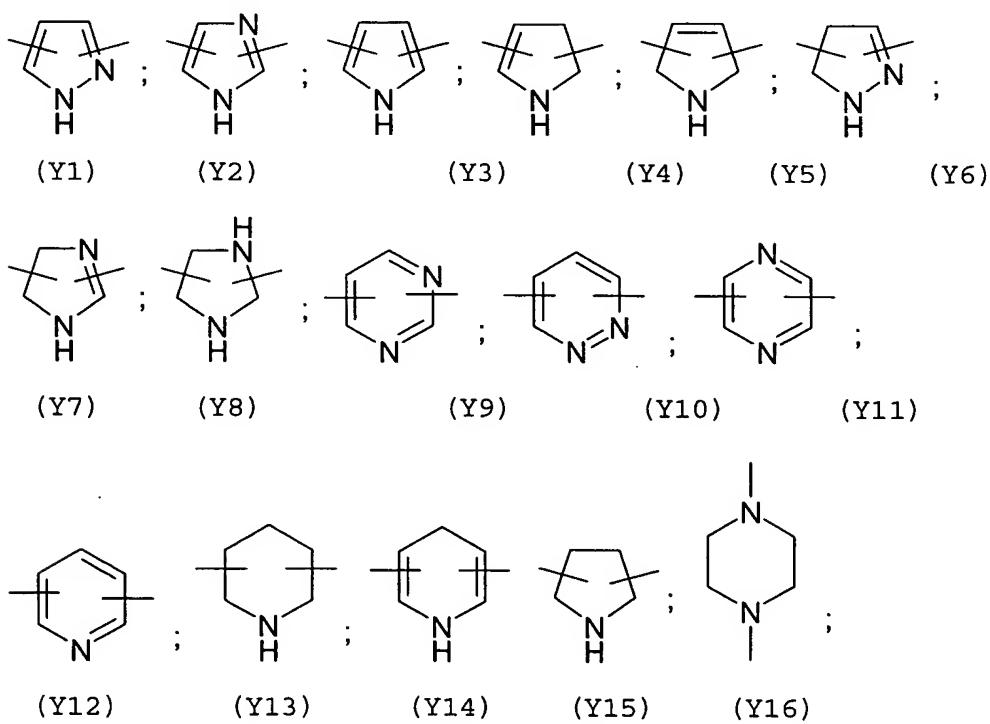
In group V), the compounds have the following meanings:

- when R is the formula (IIC),
R_{vii} is H or a C₁-C₄ linear or branched alkyl;
R_{vii-1} is R_{vii}, or C₁-C₄ linear or branched alkoxy; Cl, F, Br; the position of R_{vii-1} being ortho, or meta, or para;
the Ketorolac residue is preferred, wherein R_{vii} and R_{vii-1} are H, and T₁ = -CO-;
- when R is the formula (VIIIC),
of which the tenoxicam residue has been indicated,
T₁ = -O-;
- when R is the formula (IXC),
wherein T₁ = -O-, the piroxicam residue has been indicated;
- when R is the formula (IIIC),

wherein $T_1 = -CO-$, of which the nabumetone residue has been indicated;

- when R is the formula (IVC),
wherein $T_1 = -CO-$, of which the indomethacin residue has been indicated;
- when R is the formula (XC), the residue X is known as meloxicam; the preferred compounds are those in which $T_1 = -CO-$;
- when R is the formula (XI) the residue is known as ampiroxicam when the termination is $-CH(CH_3)OCOC_2H_5$; the preferred compounds have $T_1 = -CO-$;
- when R is the formula (XIII) and the valence is saturated with H, the residue derives from lornoxicam; the preferred compounds have $T_1 = -O-$;
- when R is the formula (XXXXV), $T_1 = -O-$ and the valence is saturated with H, the compound known as paracetamol is obtained.

5. Use according to claims 1-4, wherein in the compounds of formula (I) Y^3 of formula (III^P) of C is selected from the following bivalent radicals:



6. Use according to claim 5, wherein Y^3 is selected from the following: (Y12) with the two free valences in the ortho positions with respect to the nitrogen atom; (Y16) with the two valences linked to the two heteroatoms, Y1 (pyrazol) 3,5-disubstituted; Y16 is particularly preferred.

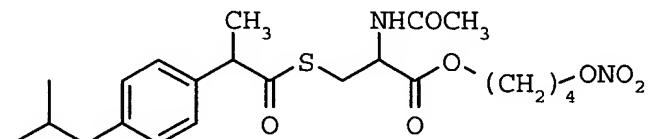
7. Use according to claims 1-6, wherein the following compounds are used:

2-acetyloxybenzoic acid 3-nitrooxymethyl phenyl ester (I^c);

2-fluoro-alpha-methyl[1,1'-biphenyl]-4-acetic acid 4-nitrooxy butylester (II^c);

2-[(2,6-dichlorophenyl)amino]benzenacetic acid 4-nitrooxy butyl ester (III^c);

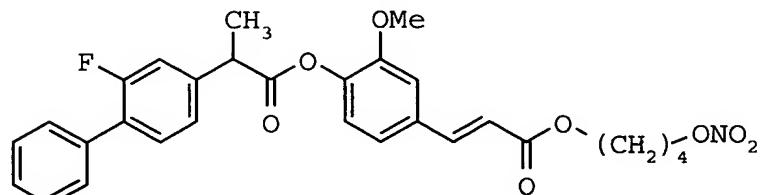
(S)-N-acetyl-[alpha-methyl-4-(2-methylpropyl)benzenacetyl] cysteine 4-nitrooxybutylester having formula:



(IV^c)

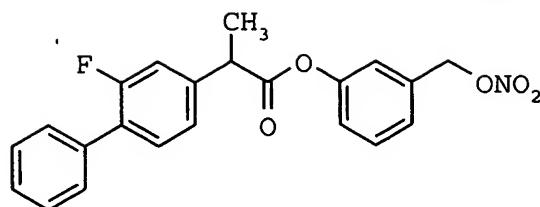
4-nitrooxybutanoic acid 4-acetylaminophenylester (V^c);

trans-3-[4-[2-fluoro-alpha-methyl(1,1'-biphenyl)-4-acetyloxy]-3-methoxyphenyl]-2-propenoic acid 4-(nitrooxy) butyl ester, having formula:

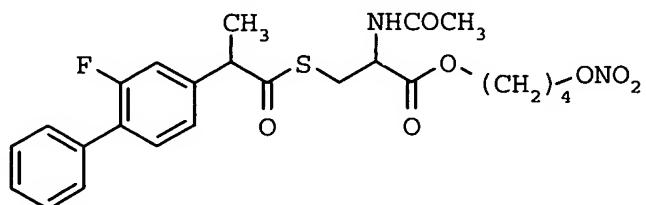


(VI^c)

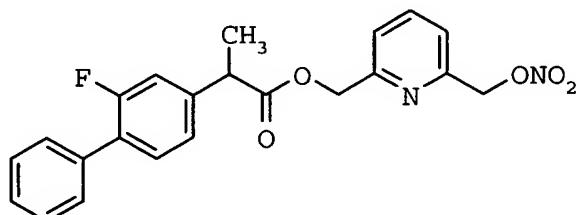
2-Fluoro-alpha-methyl[1,1'-biphenyl]-4-acetic acid 3-(nitrooxymethyl)phenyl ester having formula:

(VII^c)

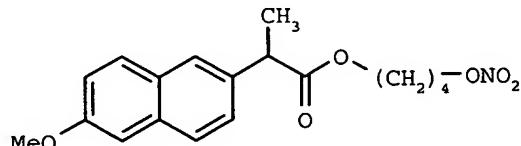
(S)-N-acetyl-[2-fluoro-alpha-methyl(1,1'-biphenyl)-4-acetyl] cysteine 4-(nitrooxy)butyl ester having formula:

(VIII^c)

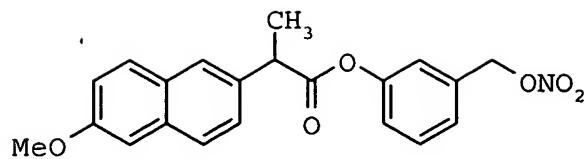
2-Fluoro-alpha-methyl[1,1'-biphenyl]-4-acetic acid 6-(nitrooxy methyl)-2-methylpyridyl ester having formula

(XI^c)

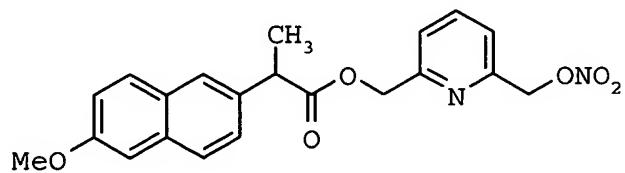
(S)-6-methoxy-alpha-methyl-2-naphthalenacetic acid 4-(nitrooxy)butyl ester having formula :

(X^c);

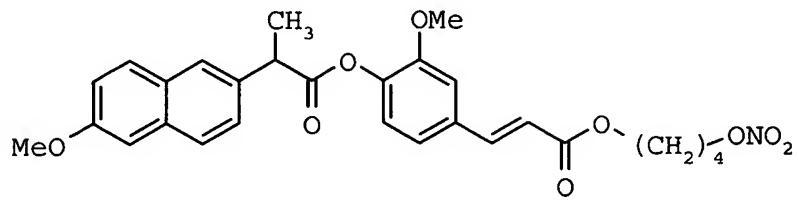
(S)-6-methoxy-alpha-methyl-2-naphthalenacetic acid 3-(nitrooxymethyl)phenyl ester having formula:

(XI^B)

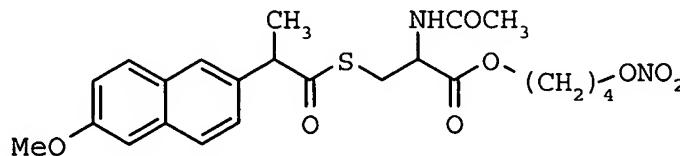
(S)-6-methoxy-alpha-methyl-2-naphthalenacetic acid 6-(nitrooxymethyl)-2-methylpyridyl ester having formula:

(XII^C)

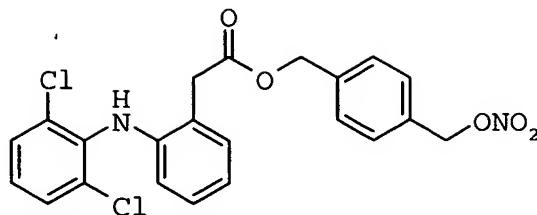
trans-3-[4-[6-methoxy-alpha-methyl-2-naphthalenacetyl oxy]-3-methoxyphenyl]-2-propenoic acid 4-(nitrooxy)butyl ester having formula:

(XIII^C)

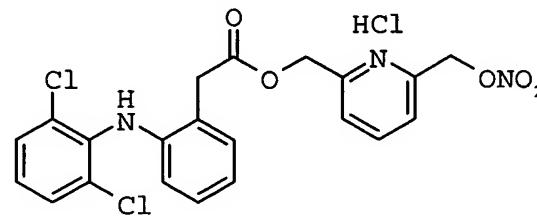
(S,S)-N-acetyl-S-(6-methoxy-alpha-methyl-2-naphthalenacetyl) cysteine 4-(nitrooxy)butyl ester having formula:

(XIV^C)

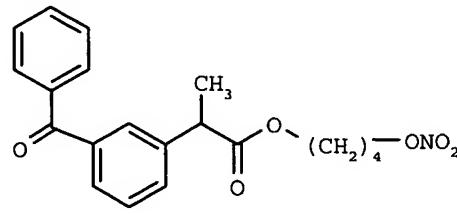
2-[(2,6-dichlorophenyl)amino]benzenacetic acid 4-(nitrooxy methyl)phenylmethyl ester having formula:

(XV^c)

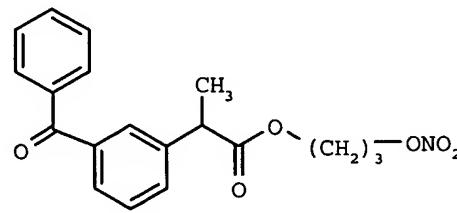
2-[(2,6-dichlorophenyl)amino]benzenacetic acid 6-(nitrooxymethyl)-2-methylpyridyl hydrochloride ester having formula:

(XVI^c)

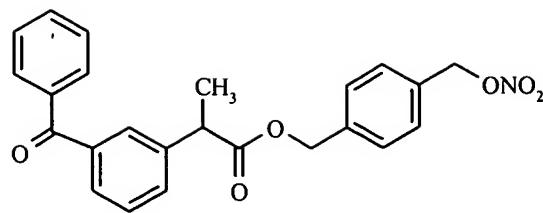
(S)-3-benzoyl-alpha-methyl-benzenacetic acid 4-(nitro oxybutyl) ester having formula:

(XVII^c)

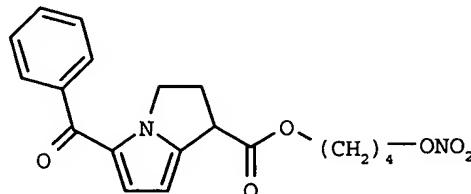
(S)-3-benzoyl-alpha-methyl-benzenacetic acid 3-(nitro oxypropyl) ester having formula:

(XVIII^c)

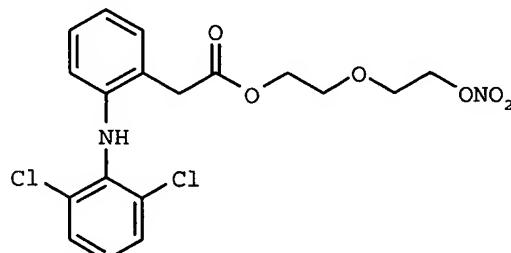
(S)-3-benzoyl-alpha-methyl-benzenacetic 4-(nitro oxy-methyl) phenylmethyl ester having formula:

(XIX^c)

5-benzoyl-2,3-dihydro-1H-pyrrolizine-1-carboxylic acid 4-(nitrooxy)butyl ester having formula:

(XXI^c)

2-[(2,6-dichlorophenyl)amino]benzenacetic acid 5-(nitrooxy)ethyloxyethyl ester having formula:

(XX^c)

1-(4-Chlorobenzoyl)-5-methoxy-2-methyl-1H-indole-3-acetic acid 3-(nitrooxymethyl)phenyl ester (XXI^c)

8. Use according to claims 1-7, wherein the compounds of formula (I) are administered in pharmaceutical formulations by oral, parenteral and topical administration.
9. Use according to claims 1-8 for the prevention of arthritis relapses